

mammal and the nucleotide sequence encoding the RNA molecule is expressed therein.

Claim 49. A plasmid comprising a DNA molecule having a first nucleotide  
5 sequence that specifically hybridizes to nucleotides 1-29574 of SEQ ID NO. 3  
under high stringency and a second nucleotide sequence encoding a bacterial  
origin of replication, wherein the first nucleotide sequence comprises ovine  
adenovirus inverted terminal repeat sequences that are linked by a third nucleotide  
sequence which contains at least one unique restriction enzyme site that is not  
10 present in the first nucleotide sequence.

### **REMARKS**

Favorable reconsideration of the subject application, as amended above, is respectfully requested in view of the comments below.

15 Claims 25-51 are pending in the present application. Claims 30 and 38 are canceled herein. Accordingly, claims 25-29, 31-37 and 39-51 are presented for examination on the merits.

The specification has been amended to correct the priority information provided on the first page of the application. Also, a typographical error on page 17  
20 of the application has also been corrected. Specifically, the specification has been amended to recite that the aovine adenovirus ITRs are 46 nucleotides in length, rather than 40 ucleotides, as is shown in SEQ ID NO. 3, nucleotides 29529-29,574.

The claims have also been amended to correct various typographical , correct dependencies and to expressly recite that which was implicit in the original claims. No new matter is added by the amendments tot he claims or specification.

Applicants have provided a new Figure 13 and a new sequence List , which  
5 includes the amino acid sequence disclosed at page 16 of the specification. The paper copy and electronic version of the Sequence List are identical and contain no new matter. Please replace the original Sequence list with the revised Sequence List enclosed herewith.

10 I. **Rejection of Claims 25-29, 31-34, 36-47 and 49-51**

Under 35 U.S.C. § 112, First Paragraph

Claims 25-29, 31-34, 36-47 and 49-51 stand rejected under 35 U.S.C. § 112, first paragraph for various reasons which are addressed beelow.

The Examiner states that support for claims 25-51 in the specification must  
15 be shown. It is respectfully submitted that each of the claims is fully supported by the specification as follows:

The original claims encompass isolated DNA molecules comprising the nucleotide sequence of the ovine adenovirus genome, and nucleotide sequences from which non-functional sequences within the ovine adenovirus genome have  
20 been removed. See original claims 1-4. The figures also provide the nucleotide sequence of the ovine adenovirus genome. At page 3, second paragraph, of the specification, it is disclosed that functional equivalent nucleic acid sequences are encompassed by the invention. At page 10, after line 15, high stringency hybridization conditions are disclosed. It is also disclosed preferably, sequences

that hybridize to the ovine adenovirus nucleotide sequence share 90% identity with the ovine adenovirus sequence. This of course, includes sequences that are variants of the

Original claims 8-11 were directed to functional plasmids containing all or portions of the ovine adenovirus genome and for example, encoding resistance to an antimicrobial agent, ITRs, or non-adenoviral sequences. More detailed disclosure of the claimed plasmids is provided at page 17 of the specification.

Original claims 12-16 were directed to adenoviral vectors of the same or similar scope as present claims 36-40.

Methods of delivering recombinant DNA molecules of the invention were set forth in original claims 17-20.

Accordingly, the present claims are fully supported by the specification.

The discrepancy between the specification at page 17 and claim 28 in regards to the length of the ovine adenovirus ITRs has been corrected.

The claims have been amended to more specifically define the invention of claims 36-40 and 43-46 as a composition or method of use comprising an adenoviral vector.

Accordingly, it is respectfully submitted that the rejection of claims 25-29, 31-34, 36-47 and 49-51 under 35 U.S.C. § 112, first paragraph, is traversed.

## **II. Rejection of Claim 41 Under 35 U.S.C. § 112, First Paragraph**

It is respectfully submitted that the amendment to claim 41 renders this ground of rejection moot.

Continuation of US 10,176,101

**III. Rejection of Claims 42-44 and 47 Under 35 U.S.C. § 112, First Paragraph**

Claims 42-44 and 47 stand rejected under 35 U.S.C. § 112, first  
5 paragraphas allegedly containing subject matter that was not described in the  
specification in such a way as to enable one skilled in the art to make and/or use  
the claimed invention. The Examiner acknowledges that the specification discloses  
that the OAV287 can infect mammalian cells of non-ovine origin. The Examiner  
also acknowledges that the specification provides evidence that the OAV287 can  
10 be used to infect sheep, and demonstrates that transfected OAV287 propagates in  
vaccinated sheep. However, the Examiner asserts that a lack of working examples  
in the specification, coupled to the unpredictable nature of the art and an alleged  
necessity for non-routine experimentation woould require undue experimantation to  
practice the invention *in vivo*.

15 Applicants respectfully disagree with the Examiner's conclusion.

Applicants have generated additional plasmids containing the infectious OAV  
genome, which were constructed using standard molecular biology techniques (9)  
and new viruses have been rescued. These plasmids further demonstrate the utility  
of OAV as a gene delivery vector. Figure 7 of the specification shows plasmid  
20 pOAV600 in which unique Apa/NotI cloning sites were inserted into a non-essential  
region of the genome. This plasmid was further modified. Nucleotides between the  
NotI and Sall sites (Figure 7) were deleted by digestion with these restriction  
enzymes and replaced by cloning in the -82bp sequence located between the NotI  
and Sall sites of the plasmid Bluescript KS<sup>+</sup> (Stratagene, La Jolla, CA). This deleted  
25 1938 nucleotides from the OAV genome and created plasmid pOAV603 (Figure13),

Plasmid pOAV209 (Figure 13) was constructed by subcloning the XbaI-cut pACYC184 (4,244bp) into the XbaI site of Bluescript KS<sup>+</sup>. The fragment was then excised using flanking ApaI and NotI sites and subcloned into ApaI/NotI-cut pOAV200 (Figure 7). Plasmids; pOAV209 (Amp<sup>R</sup>/Cm<sup>R</sup>) and pOAV603 were characterized by digestion with restriction enzymes. pOAV287Cm (Figure 6) and pOAV209 contain the same -4.2kb "stuffer" DNA fragment from pACYC184. For the former, the fragment was cloned into the unique Sall site of the OAV genome. Plasmid pOAV623 contains a gene cassette comprising an enhancer element derived from the prostate specific membrane antigen, gene linked to the rat probasin promoter and the purine nucleoside phosphorylase gene derived from E. coli. This cassette of total size -2.4kb was cloned into the ApaI/NotI siteA of pOAV600 in the left to right orientation. Based on the transcription map of OAV that it has been determined that the cassette in pOAV623 is located between the transcription units for the left end and proposed E4 regions of the OAV genome. (Khatri and Both, 1998). In addition, a cassette comprising the Rous Sarcoma virus LTR linked to the human alpha-1-antitrypsin cDNA and bovine growth hormone polyadenylation signal was cloned into the ApaI/NotI sites of pOAV200 in the right to left orientation (pOAVhAAT, Figure 13), which is the opposite orientation compared with all other cassettes. These plasmids were digested with KpnI or its isoschizomer, Asp718 to release the linear genome. The DNAs were individually transfecting into CSL503 cells using methods described at page 13, line 5-23 of the specification. The viruses corresponding to the plasmids described in Figure 13 were rescued, characterized by restriction enzyme digestion and shown to have the correct structure.

The rescue of these viruses identifies additional useful properties of the OAV vector. Two new non-essential sites for the insertion of foreign DNA have been identified. The *Apal*/*NotI* cloning sites in pOAV600 (Figure 7) have been shown to be suitable for the construction of a recombinant virus by the rescue of OAV623 (Figure 13). The *Sall* site near the right end was identified in pOAV600S (Figure 7) as non-essential (page 19, line 34-page 20, line 6). The foreign DNA (from pACYC184) carried by pOAV287Cm (Figure 7) was inserted in a non-essential region, which was confirmed by the fact that the corresponding virus, OAV297Cm, was rescued (Figure 13). A similar virus (OAV209, Figure 13) in which the same pACYC184 DNA was inserted between the pVH and fiber genes was also rescued. Thus, these data show that the OAV capsid can package at least 4.23kb of foreign DNA, *i.e.*, 114% of the wild type genome, in either of two sites without a compensation deletion. This capacity is significantly greater than that of human adenovirus type 5 (Bett et al.1993) and is large enough to accommodate many individual genes of interest to researchers.

In addition, -2kb of non-essential sequences have been identified in the OAV genome. Surprisingly, four of six potential open reading frames in the transcription unit designated as RE in Figure 13 are closely related to each other and may have redundant functions (Xu et al., 1997). In confirmation of this, deletion of all but one of these reading frames in pOAV603 still allows the rescue of a viable virus. Thus, deletion of these sequences coupled with the ability to insert at least 4.23kb of DNA means that OAV has capacity to carry at least 6.3kb of foreign DNA,

The construction of recombinant virus OAV205 (Figure 10) is broadly described on page 21 lines 19-33. More specifically, pOAV205 was constructed by

subcloning a gene fragment encoding the 45W antigen from the sheep parasite *Taenia ovis*. The gene fragment, excised as an EcoRI/BamHI fragment, was linked to the OAV MLP/TLS sequences (page 21, lines 13-21) in plasmid pMT (Figure 9) cut withHindIII/BglII via a HindIII/EcoRI adapter. The adapter also provided an  
5 in-frame ATG codon. The MLP/TLS/45W cassette was excised as an ApaI/NotI fragment and subcloned into pOAV200 (Figure 10). The virus expresses the antigen known as 45WB/X in CSL503 cells infected *in vitro* (Figure IIA). This virus was used to vaccinate sheep, alone, or in combination with a purified plasmid, pcDNA3-45W (Rothel et al., 1997) that expressed the 45W antigen, or with purified  
10 45W-GST fusion protein that had been expressed in *E. coli* (Lightowers et al., 1996). Dorset X Merino wethers and ewes that were 10-12 months of age at the time of first vaccination were inoculated intramuscularly with plasmid (200ug/dose in a total volume of 1 ml of phosphate-buffered saline), 45W-GST (50 ug/dose formulated with Quil A adjuvant (Supcrfos, Demnark; 1mg/dose). For both primary  
15 and secondary inoculations wild-type OAV or recombinant OAV205 was given intra-muscularly ( $-2 \times 10^8$  pfu), intra-nasally ( $-3.4 \times 10^7$  pfu) and intra-conjunctivally ( $-1.7 \times 10^7$  pfU), There was a 4-week gap between primary and secondary inoculations. Antibody formation (classes IgG1 and IgG2) against 45W protein was detected by ELISA (Rothel et al., 1996),

20 In a pilot experiment, two of the sheep inoculated with OAV205 developed low levels of 45W-specific serum antibody titres ( $<200$ ), whereas specific antibody could not be detected in sera from animals inoculated with wild type OAV. In a larger experiment animals were vaccinated as shown in Table 1. Sheep vaccinated with two doses of either the plasmid DNA or OAV205 vaccines elicited low levels of

45W specific antibody with the adenovirus vector proving more effective (Figure 14). Animals vaccinated with OAV205 mounted predominantly an IgG1 response that was maximal two weeks after the primary vaccination. This was not further boosted by revaccination at 4 weeks. For all sheep that received the OAV205, low  
5 levels of OAVspecific antibody were detected in sera collected two weeks after the second vaccination. The mean OAV-specific IgG titer for these animals was 548 (+/-486) with a range of 120-2000.

Although animals vaccinated with OAV205 elicited low levels of 45W-specific antibody they were primed to generate an enhanced immune response after  
10 subsequent vaccination with 45W/Quil A (Figure 15, compare B and D with A). The IgG<sub>1</sub> titres for D are significantly higher than for A (Mann-Whitney U=17, P<0.05). Similarly, vaccination with OAV205 can boost an immune response primed with protein/Quil A (Figure 15, compare A with C).

In addition, an immune response primed by vaccination with plasmid DNA is  
15 boosted by OAV205. Animals from group 9 (Table 1) generated high levels of 45W-specific antibody that was predominantly of the IgG1 isotype. All three sheep had low but detectable titers after the second DNA vaccination (titers of 110, 140 and 150). One week after vaccination with OAV205 the mean IgG<sub>1</sub> titer was 9367, a level >65 fold higher than that in sheep receiving two inoculations of either DNA or  
20 OAV205 alone and comparable to the levels achieved with two inoculations of protein/Quil A (mean titer 11833).

A challenge experiment was carried out to ascertain whether the antibody levels generated by the various vaccination procedures were protective against *Taenia ovis*, the parasite from which the 45W antigen was derived. Eight weeks



after their final vaccination animals from groups 1, 2, 3, 9 and 10 (Table 1) were challenged by intraruminal injection of *T. ovis* 5000 eggs. A further four weeks later these sheep, were killed and their heart, diaphragm, masseters and the muscle tissue of their right rear legs (vaccination site) was examined for the presence of cysticerci by slicing the tissues at 3mm intervals.

Sheep sequentially immunized with plasmid DNA and boosted with OAV205 were significantly protected from *T. ovis* challenge (Table 1) (Mann-Whitney U=19, P=0.02). Similarly, sheep initially vaccinated with protein/Quil A (group 2) were protected (U=17.5, P, 0.05). As a group the animals that received two inoculations with protein/Quil A (group 1) were not significantly protected (P=0.078). This was probably a reflection of the 45W-specific antibody levels in two of these sheep that dropped to non-protective levels by the time of challenge. In addition, the two surviving sheep in group 3 (Table 1) had only low 45W-specific antibody levels at the time of challenge and were not protected. Overall there was a significant inverse correlation between 45W-specific IgG1 titers and cyst numbers (Pearson correlation P<0.05). However, there was no correlation between cyst numbers and 1902 levels (P=0.52).

In summary, these data show that the ovine adenovirus vector OAV205 is capable of delivering a gene for a parasite antigen to sheep such that a measurable immune (antibody) response is induced. Further, the recombinant vector primes an immune response that can be boosted by vaccination with the recombinant protein. The vector can also be used to boost an immune response primed by 45W plasmid DNA or protein/Quil A vaccine. Combination vaccination strategies are able to induce a protective immune response against a sheep parasite.

## Additional references

Bett, A. J., Prevec, L., and Ghaham, F. L. (1993). Packaging capacity and stability of human adenovirus type-5 vectors. *J Virol* 67(10), 5911-5921,

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Khatri, A., and Both, G. W. (1998). Identification of transcripts and promoter regions of ovine adenovirus OAV287, *Virology* 245(1), 128-141.

Lightowers, M. W., Waterkeyn, J. G., Rothel, J. S., Gauci, C. G., and Harrison, G. B. (1996). Host-protective fragments and antibody binding epitopes of the *Taenia ovis* 45W recombinant antigen, *Parasite Immunology* 18(10), 507-13.

Rothel, J. S., Lightowers, M. W., Scow, H. F., Wood, P. R., Rothel, L. I., Heath, D. D., and Harrison, G. B. (1996). Immune responses associated with protection in sheep vaccinated with a recombinant antigen from *Taenia ovis*. *Parasite Immunology* 18(4), 201-8.

Rothel, J. S., Waterkeyn, J. G., Strugnell, R. A., Wood, P. R., Scow, H. F., Vadolas, J., and Lightowers, M. W. (1997). Nucleic acid vaccination of sheep: Use in combination with a conventional adjuvanted vaccine against *Taenia ovis*. *Immunol Cell Biol* 75, 41-6.

Xu, Z. Z, Hyatt, A., Boyle, D. B., and Both, O. W. (1997). Construction Of Ovine Adenovirus Recombinants By Gene Wertion And Deletion Of Related Terminal Sequences. Virology 230, 62-71.

5 Figure legends (for figures provided herein).

Figure 13. Structure of OAV genomes in several new recombinant viruses. The viruses were rescued from the corresponding plasmids in which sequences from a modified Bluescript plasmid linked the ends of the viral genome as shown in Figure 7 and described on p.12, lines 23-36 of the specification

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Figure 14. Mean 45W-specific IgG, (circles) and IgG2 (squares) ELISA titers of sheep vaccinated with either pcDNA-45W (diamonds) or recombinant OAV205 (squares). The three sheep per group were vaccinated at week 0 and revaccinated at week 4.

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Figure 15. Mean 45W-specific IgG<sub>1</sub> (solid bars O and IgG2 (hatched bars) ELISA titers of sheep vaccinated with various combinations of vaccine delivery systems, Values are the mean titers (with standard errors) for each vaccine group measured in sera collected two weeks after the last vaccination. Animals were vaccinated as follows: A, protein/Quil A; B, protein Quil A twice, four weeks apart; C, protein Quil A, followed by OAV205; D, OAV205 followed by protein/Quil A.

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Table 1. Vaccination of sheep with various combinations of vaccine delivery systems and number of *T. ovis* cysticerci found four weeks after a challenge

infection.

	Sheep No.	Group	Vaccine	IgG <sub>1</sub> titre	IgG <sub>2</sub> titre	No. cysts
	21	1	1° protein/Quil A	#360	#400	62
5	41	1	20 protein/Quil A	2400	1500	1
	43	1		2500	2000	1
	78	1		15000	13000	0
	79	1		1050	550	34
	93	1		1100	110	3
10	45	2	1° protein/Quil A	2100	2200	2
	93	2	2° Adeno	4000	1700	0
	95	2		4100	7400	0
	73	3	1° Adeno	890	0	ND*
	85	3	2° protein/Quil A	1100	700	18
15	97	3		1200	2050	26
	23	9**	1° DNA	4700	1800	0
	74	9	2° DNA	7000	750	0
	87	9	3° Adeno	9000	690	1
	24	10	Nil	180	0	99
20	25	10		0	0	129
	26	10		0	0	111
	42	10		0	180	24
	80	10		130	0	17
	94	10		0	0	2

# 45W-specific IgG<sub>1</sub> and IgG<sub>2</sub> ELISA titers are shown for sera collected at the time of challenge infection.

\* Sheep number 73 died prior to the assessment of the *T. ovis* challenge infection from causes which were unrelated to the experimental protocol.

5   \*\* These animals were inoculated with OAV205 five weeks after the second vaccination.

Based on the above information, it is evident that the claimed DNA, plasmid, vector and methods provide therapeutic benefit.

Accordingly, the rejection of claims 42-44 and 47 under 35 U.S.C. § 112, first  
10 paragraph is respectfully traversed.

15   **IV. Rejection of Claims 25-27, 33, 34, 36-47 and 49 Under 35 U.S.C. § 112, Second Paragraph**

It is respectfully submitted that the amendments to the claims render these grounds of rejection moot.

20   **V. Rejection of Claims 25-28, 30-33, 36-41, 46 and 48 Under the Judicially Created Doctrine of Obviousness-type Double Patenting**

Applicants have enclosed a Terminal Disclaimer, disclaiming portion of the of the statutory term of any patent granted on the instant application, which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. 154 to 156  
25 and 173, as presently shortened by any terminal disclaimer, of prior U.S. Patent No. 6,020,172.

It is respectfully submitted that the subject application, as amended above, is in condition for allowance, an early notification thereof being earnestly solicited.

Please charge any additional fees or credit any overpayment in connection with this communication to deposit Account 50-0417.

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Respectfully submitted,

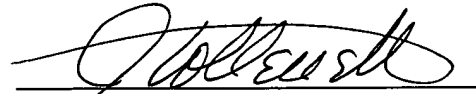
McDERMOTT, WILL & EMERY

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Dated:

March 17, 2003

By:



Judith L. Toffenetti

Registration No. 39,048

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600 13th Street, N.W., Suite 1200

Washington, D.C. 20005-3096

Telephone: (202) 756-800

Facsimile: (202) 756-8087

Continuation of 09/464,767

## **MARKED UP VERSION SHOWING CHANGES MADE**

### **IN THE SPECIFICATION:**

5        *On page 1 of the specification following the title, the first paragraph has been amended as follows:*

         This application is a [Continuation Application of parent application, Serial No.09/464,767, which is a] Continuation-In-Part Application of Serial No. 08/776,274, filed January 24, 1997, (abandoned) as the National Phase of PCT  
10    Application No. PCT/AU95/00453, filed July 26, 1995 and claiming priority to Australian Application No. PM7101, filed July 26, 1994.

15        *On page 16, line 3 of the specification the following paragraph has been amended as follows:*

         (b) in other adenoviruses the E4 region is normally located at the right-hand end of the genome. the OAV287 E4? region is tentatively identified based only on the presence of a protein sequence motif HCHC ... PGSLQC (SEQ ID NO. 4) which is found in 18.8 kD and 30.85 kD orfs in this region. Identical or very similar  
20    motifs are found in the E4 34 kD protein of human Ad2 and Ad40 and mouse adenoviruses;

*On page 17, line 18, the following paragraph has been amended as follows:.*

         The circular genome clone differs from the naturally occurring circles that  
25    occur in Ad5-infected cells (10) and that might exist in OVA2887-infected cells in that the [40] 46 base pair ITRs are joined by a GATC linker. Together with the last and first nucleotides of the genome (G and C, respectively, see Figure 1), this

sequence forms a unique KpnI site when the ITRs are joined head to tail. Other sites such as EcoRI, BamHI, Sall, KsaI, etc. which have recognition sequences beginning with G and ending with C are suitable if they are unique as the 3' and 5' terminal nucleotides of other adenovirus genomes are G and C, respectively. A plasmid with a suitable antibiotics resistance gene e.g. amp<sup>R</sup> and origin of replication can be inserted at the unique site or elsewhere in the genome to form a plasmid which can be propagated in bacteria. Plasmids propagated in the presence of 200 µg/ml ampicillin in *E. coli* strains JM109 and DH5-alpha retain the KpnI sites and inserted sequences, indicating that the OAV287 ITR sequences are stable when linked in this manner. This approach may therefore be used to engineer other adenovirus genomes. If desired the GATC linker sequence can be removed and the authentic termini regenerated prior to transfection by digestion with KpnI (or other appropriate enzyme) and incubation with T4 DNA polymerase to create blunt ends (9).

**IN THE CLAIMS:**

*Please cancel claims 30 and 38 in their entirety and without prejudice.*

*Please amend claims 25-27, 29, 31, 35-37, 39-47 and 49 as follows.*

Claim 25. An isolated DNA molecule comprising nucleotides 1-29,574 of SEQ ID NO. 3 or an isolated DNA molecule that hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. 3 under high stringency conditions [and which encodes a functional ovine adenovirus genome].



Claim 26. The isolated DNA molecule of claim [1] 25, wherein the DNA molecule specifically hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. [13] 3 and shares at least 90% identity therewith.

5 Claim 27. The isolated DNA molecule of claim 25, wherein the nucleotide sequence is a variant of nucleotide 1-29,574 of SEQ ID NO. 3, which comprises at least one nucleotide difference in the [ovine adenovirus genome] sequence that does not alter the amino acid sequences encoded thereby.

10 Claim 29. An isolated DNA molecule [having a nucleotide sequence which specifically hybridizes under high stringency conditions to the complement nucleotide 1-29,574 of SEQ ID NO. 3, wherein the DNA molecule comprises an ovine adenovirus genome from which all or part of a] comprising nucleotides 1-29,574 of SEQ ID NO. 3 with the exception that the DNA molecule has all or part of  
15 the non-essential portion encoding genetic information that is not essential to the maintenance or viability of ovine adenovirus (OAV287) [has been] deleted or altered, said non-essential portion comprising an open reading frame comprising nucleotides 28487 through nucleotide [29014] 29044 of the complement of SEQ ID NO. 3 or an open reading frame comprising nucleotides [28511] 28541 through  
20 nucleotide [28699] 28729 of the complement of SEQ ID NO. 3.

Claim 31. A plasmid comprising a bacterial origin of replication and a first nucleotide sequence as set forth in nucleotides 1-29,574 of SEQ ID NO. 3 or a second nucleotide sequence that specifically hybridizes to the complement of

nucleotides 1-29,574 of SEQ ID NO. 3 under high stringency conditions [and which comprises a functional adenovirus genome].

Claim 35. The plasmid of claim 33 [or 34] wherein the third nucleotide  
5 sequence encodes resistance to an antimicrobial agent.

Claim 36. [A] An adenoviral vector comprising (1) a first nucleotide  
sequence having the sequence as set forth in nucleotides 1-29,574 of SEQ ID NO.  
3 or a second nucleotide sequence that specifically hybridizes to the complement of  
10 nucleotides 1-29,574 of SEQ ID NO. 3 under high stringency conditions and (2) a  
third nucleotide sequence encoding at least one non-adenoviral polypeptide  
[operatively linked to the first or second nucleotide sequence].

Claim 37. The adenoviral vector of claim 36, wherein the second  
15 nucleotide sequence specifically hybridizes to the complement of nucleotides 1-  
29,574 of SEQ ID NO. 3 and shares at least 90% identity therewith.

Claim 39. The adenoviral vector of [any one of claims 35-36] claim 36 or  
37, wherein the non-adenoviral polypeptide is a bacterial, viral, parasite or  
20 eucaryotic polypeptide.

Claim 40. The adenoviral vector of claim 39, wherein the non-adenoviral  
polypeptide is selected from rotavirus VP7sc antigen, *Trichostrongylus*

*colubriformis* 17 kD antigen, *Taenia ovis* 45W antigen and *Lucila cuprina* PM95 antigen.

Claim 41. A method of delivering a DNA molecule encoding at least one  
5 non-adenoviral polypeptide to a mammalian target cell comprising transfecting the  
target cell with an adenoviral vector comprising (1) a first nucleotide sequence set  
forth in nucleotides 1-29,574 of SEQ ID NO. 3 or a second nucleotide sequence  
that hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. 3 under  
high stringency conditions[and which comprises the ovine adenovirus genome]; and  
10 (2) a third nucleotide sequence encoding at least one non-adenoviral polypeptide,  
wherein the at least one polypeptide is expressed in the target cell.

Claim 42. A method of delivering a DNA molecule encoding at least one  
non-adenoviral polypeptide to [an animal] a mammal comprising administering to  
15 the [animal] mammal an adenoviral vector comprising (1) a first nucleotide  
sequence as set forth in nucleotides 1-29,574 of SEQ ID NO. 3 or a second  
nucleotide sequence that specifically hybridizes to the complement of nucleotide 1-  
29,574 of SEQ ID NO. 3 under high stringency conditions [and which comprises the  
ovine adenovirus genome]; and (2) a third nucleotide sequence encoding at least  
20 one non-adenoviral polypeptide, wherein the adenoviral vector transfects at least  
one cell of the [animal] mammal and the at least one polypeptide is expressed  
therein.

Claim 43. The method of claim 42, wherein the adenoviral vector is administered to a grazing mammal.

Claim 44. The method of claim 43, wherein the adenoviral vector is  
5 administered to a sheep.

Claim 45. [A] An adenoviral vector comprising (1) a first nucleotide as set forth in SEQ ID NO. 3 or a second nucleotide sequence that specifically hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. 3 under high stringency  
10 conditions [and which comprises the ovine adenovirus genome]; and (2) a nucleotide sequence encoding an RNA molecule.

Claim 46. The adenoviral vector of claim 45, wherein the RNA molecule is an antisense RNA molecule or ribozyme.  
15

Claim 47. A method of delivering a DNA molecule encoding a functional RNA molecule to [an animal] a mammal comprising administering to the [animal] mammal [a] an adenoviral vector comprising (1) a first nucleotide sequence as set forth in SEQ ID NO. 3 or a second nucleotide sequence that specifically hybridizes  
20 to the complement of nucleotides 1-29,574 of SEQ ID NO. 3 under high stringency conditions [and which comprises the ovine adenovirus genome]; and (2) a nucleotide sequence encoding an RNA molecule, wherein adenovirus vector transfects at least one cell of the [animal] mammal and the nucleotide sequence encoding the RNA molecule is expressed therein.

Claim 49. A plasmid comprising a DNA molecule having a first nucleotide sequence that specifically hybridizes to nucleotides 1-29574 of SEQ ID NO. 3 under high stringency [and which comprises the ovine adenovirus genome] and a  
5 second nucleotide sequence encoding a bacterial origin of replication, wherein the first nucleotide sequence comprises ovine adenovirus inverted terminal repeat sequences that are linked by a third nucleotide sequence which contains at least one unique restriction enzyme site that is not present in the first nucleotide sequence.

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